

Associations of depression with diet in a prospective intervention study

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Tiivistelmä – Referat – Abstract <p>Objective. Depression is associated with increased risk of chronic disease, which may be at least partly due to poor health behaviors. Growing body of evidence has associated depression with unhealthy diet. However, the association of depression with diet quality in the long run is not well known. Furthermore, it is unclear if dietary interventions could mitigate the harmful association of depression with diet. This study examined the association of depression with diet both cross-sectionally and longitudinally in a population-based prospective cohort. The effectiveness of an early-onset dietary intervention in modifying these associations was investigated.</p> <p>Methods. The sample (n = 457) was from The Special Turku Coronary Risk Factor Intervention Project (STRIP). The intervention group (n = 209) had undergone a dietary intervention lasting from age of 7 months until age of 20 years. Depression was measured at age 20 using Beck Depression Inventory II (BDI-II). Diet quality was assessed at ages 20 and 26 using a diet score calculated based on food diaries. Missing values were replaced using multiple imputation by chained equations. Linear regression analyses were used to analyze the association of depression at age 20 with diet at ages 20 and 26, as well as the modifying effect of intervention group on these associations.</p> <p>Results. No cross-sectional association was found for depression and diet at age 20. Depression at age 20 was longitudinally associated with worse diet quality at age 26. The associations did not differ between intervention and control groups at either of the time points.</p> <p>Conclusions. Contrary to previous research, this study did not find cross-sectional association for depression with diet. However, this study offers novel information on longitudinal associations, suggesting that depression may have effects on diet quality that can manifest after several years. Dietary intervention was not found effective in modifying these associations. Since long-term effects on diet may be an important factor explaining the association of depression with chronic diseases, ways to mitigate the adverse consequences of depression for diet should be explored further.</p>			
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Tiivistelmä – Referat – Abstract <p>Tavoitteet. Masennus on yhteydessä moniin kroonisiin sairauksiin, ja yhteyden ajatellaan selittyvän ainakin osin terveyskäyttäytymisellä. Viime vuosien tutkimuksen perusteella masennus näyttäisi olevan yhteydessä epäterveelliseen ruokavalioon. Ei kuitenkaan tiedetä, miten masennus vaikuttaa ruokavalioon pitkällä aikavälillä. On myös epäselvää, voidaanko intervention keinoin vaimentaa masennuksen haitallisia vaikutuksia syömiskäyttäytymiseen. Tässä tutkimuksessa selvitettiin, onko masennus yhteydessä ruokavalion laatuun samassa aikapisteessä tai kuusi vuotta myöhemmin väestöpohjaisessa kohorttiaineistossa. Lisäksi selvitettiin, vaimentaako varhain aloitettu ruokavaliointerventio masennuksen yhteyttä epäterveelliseen ruokavalioon.</p> <p>Menetelmät. Otos (n = 457) koostui The Special Turku Coronary Risk Factor Intervention Project (STRIP) -interventiotutkimuksen osallistujista. Interventoryhmä (n = 209) oli saanut ruokavalio-ohjausta 7 kuukauden iästä 20 vuoden ikään saakka. Masennusoireet arvioitiin 20-vuotiaana Beck Depression Inventory II (BDI-II) -kyselylomakkeella. Ruokavalion laatua arvioitiin 20- ja 26-vuotiaana ruokapäiväkirjoihin pohjautuvalla pisteytyksellä. Aineistosta korvattiin puuttuvia arvoja käyttäen moni-imputointia. Lineaaristen regressiomallien avulla analysoitiin 20-vuotiaana mitatun masennuksen yhteyttä ruokavalioon 20- ja 26-vuotiaana, sekä interventoryhmän vaikutusta näihin yhteyksiin.</p> <p>Tulokset. 20-vuotiaana mitattu masennus ei ollut yhteydessä ruokavalion laatuun samanikäisenä. 20-vuotiaana mitattu masennus oli yhteydessä epäterveellisempään ruokavalioon 26-vuotiaana. Masennuksen ja ruokavalion yhteyksissä ei ollut eroa interventio- ja kontrolliryhmän välillä kummassakaan aikapisteessä.</p> <p>Johtopäätökset. Tässä tutkimuksessa masennus ei ollut yhteydessä ruokavalioon samassa aikapisteessä, mikä on ristiriidassa aiemman tutkimusnäytön kanssa. Tutkimus tarjoaa kuitenkin uutta tietoa masennuksen pitkäaikaisista yhteyksistä syömiskäyttäytymiseen, sillä masennuksen havaittiin ennustavan epäterveellistä ruokavaliota kuusi vuotta myöhemmin. Ruokavaliointerventio ei havaittu vaikuttavan masennuksen ja ruokavalion välisiin yhteyksiin. Masennuksen pitkäaikaiset vaikutukset syömiskäyttäytymiseen voivat olla tärkeä masennuksen yhteyttä sairausriskiin selittävä tekijä, ja tulevaisuudessa on tärkeä selvittää keinoja masentuneiden ruokavalion laadun parantamiseksi.</p>			
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1 Introduction

Depression is a significant public health issue: its estimated worldwide prevalence was 4,4 % in 2015 and it is the largest cause of nonfatal health loss measured as Years Lived with Disability (YLD) (WHO, 2017). Depression itself has major effects on quality of life and general well-being. In addition, depression is highly comorbid with several chronic physical diseases (Scott et al., 2016). Depression has been shown to increase the risk of cardiovascular disease, stroke, type 2 diabetes, metabolic syndrome and obesity, and possibly the risk of Alzheimer's disease and even cancer (Clarke & Currie, 2009; Elderon & Whooley, 2013; Penninx, Milanechi, Lamers & Vogelzangs, 2013; Matta et al., 2019). Patients with depression also have an increased risk for greater disease severity, longer hospital stays and increased disease mortality (Clarke & Currie, 2009).

Why is depression associated with increased risk of chronic diseases? Many underlying mechanisms have been suggested, including stress-related hyperactivity of hypothalamic-pituitary-adrenal (HPA) axis, low heart rate variability, systemic inflammation, lifestyle factors and noncompliance with medical regimen (Elderon & Whooley, 2013; Joynt, Whellan & O'Connor, 2003; Penninx et al., 2013). According to a review by Elderon & Whooley (2013), low heart rate variability, systemic inflammation and poor health behaviors are the only factors mediating the effect of depression on increased risk of cardiovascular disease that are strongly supported by scientific evidence. In addition to their independent connection with chronic diseases, poor health behaviors can also contribute in development of systemic inflammation and low heart rate variability (Berk et al., 2013; Elderon & Whooley, 2013; Penninx et al., 2013). Thus, health behaviors, such as diet quality, represent an important factor in understanding the connection between depression and chronic diseases.

In modern food environments, the consumption of energy dense and processed foods high in sugar and salt has increased whereas the consumption of whole foods such as vegetables, fruits and legumes has decreased (Zobel, Hansen, Rossing & von Scholten, 2016). In general population, the association of unhealthy diet with chronic disease risk is well known. The symptoms of depression have also potential effects on making compliance to healthy diet even more difficult. Psychological stress has been suggested to affect appetite and increase the rewarding effect of palatable foods via glucocorticoid signaling (Adam & Epel, 2007). It has also been hypothesized

that food may be used as a self-medication in psychological distress. Palatable foods can bring a relief by temporarily decreasing HPA-axis activity (Adam & Epel, 2007). High-carbohydrate foods increase serotonin secretion by increasing the amount of tryptophan in the brain which can have temporary positive effects on mood (Wurtman & Wurtman, 1995). In addition, the so-called emotional eating style has been researched, where food has been suggested to be used as a maladaptive emotion regulation strategy (Evers, Stok & Ridder, 2010; Konttinen, Männistö, Sarlio-Lähteenkorva, Silventoinen & Haukkala, 2010; van Strien, Konttinen, Homborg, Engels & Winkens, 2016). Given that eating behaviors may play an important role in linking depression to lifestyle diseases, it is important to investigate if depression is indeed associated with unhealthy diet.

1.1 Depression and overall diet quality

Research examining the relationship between diet and depression has mainly focused on whether poor diet is a risk factor of depression. According to recent meta-analyses, unhealthy diet seems to be associated with a greater risk of depression (Li et al., 2017; Molendijk, Molero, Sánchez-Pedreño, Van der Does & Martínez-González, 2018; Nicolaou et al., 2019). However, majority of these studies are based on correlations between diet and depression and therefore cannot demonstrate causality. In a 2013 systematic review, Quirk et al. found that there were only three studies using depression as a predictor of diet quality, and the results of these studies were conflicting. In two of these studies depressive symptoms were connected to a lower likelihood of adhering to a healthy diet, one study found a connection in white but not in black individuals, and one study did not find any connection.

Since the review by Quirk et al. (2013), the number of studies investigating if depressive symptoms predict diet quality has increased. These studies are summarized in Table 1. In majority of the studies, depression has been associated with worse diet quality. Out of ten studies, four studies found that depressed participants were less likely to have healthy diet compared to non-depressed participants (Jacka et al., 2015; Errisuriz et al., 2019; Paans et al., 2019; Matta et al., 2019). In four studies, number of depressive symptoms/depression severity predicted worse diet quality linearly (Appelhans et al., 2012; Sinclair, 2016; Gibson-Smith, Bot, Brouwer, Visser & Penninx, 2018; Paans et al., 2019). In one study, chronic or recurrent depression was associated with worse diet quality (Elstgeest et al., 2019a). One study did not find association between

depression severity and diet quality (Rahe et al., 2015). However, in this study by Rahe et al. (2015), participants with atypical depression had worse diet quality than those with melancholic depression or no depression. Only one study did not find any connection between depression and diet quality (Jaalouk, Boumosleh, Helou & Jaoude, 2019).

Research conducted so far suggests that depression is a risk factor for worse overall diet quality. However, research on the topic is still quite scarce, and there are some limitations that need to be considered when interpreting the evidence. Most of the studies have been conducted in western societies (United States, Australia and Western Europe) so the findings may not generalize on different populations. Two studies made in Fiji and Lebanon show conflicting results (Sinclair, 2016; Jaalouk et al., 2019). There are also some methodological inconsistencies that may impact the comparability of different studies. For example, some of the studies have used known pre-existing diet scores in the assessment of diet quality, whereas some have used diet patterns created from the data with exploratory factor analysis. There are also differences in the definitions and assessment of depression or depressive symptoms and cut points used in each study. Furthermore, studies have focused on cross-sectional associations between depressive symptoms and diet quality, no studies were found that would have investigated longitudinal effects of depressive symptoms on overall diet quality. Although depression has been associated with worse diet quality in many studies, since these studies are observational in nature, they cannot confirm causal relationship between depression and diet quality. Depression could be a risk factor for unhealthy diet, or unhealthy diet could be a risk factor for depression as suggested by previous literature (Li et al., 2017; Molendijk et al., 2018; Nicolaou et al., 2019). It is also possible, that associations between depression and diet are bidirectional.

Table 1: Research examining associations of depression with overall diet quality

Author, year, country	n (% Women)	Mean age (±SD/range)	Population description	Depression assessment	Dietary assessment	Summary of associations	Adjusted for confounders
Appelhans et al., 2012 (US)	161 (100)	45.9 (10.8)	Women with comorbid MDD and obesity	BDI-II, HRSD	Three 24 h diet recalls, AHEI	Greater depression severity was associated with poorer diet quality (B = -0.26)	Depression-related appetite change, BED, income, education, age, BMI, antidepressant use
Jacka et al., 2015 (Australia)	3668 (55.5)	Age groups 20's 40's and 60's	Randomly recruited participants of the Personality and Total Health (PATH) Through Life Study	Goldberg Depression Scale	FFQ, Dietary patterns by principal components	Current depression was associated with less healthy diet (lower score on prudent dietary pattern) (B = -0.12)	Age group, gender, socioeconomic position, cardiovascular risk factors, health behaviours
Rahe et al., 2015 (Germany)	1660 (54.9)	Depressed: 49.4 (43.9-55.6) Controls: 53.5 (46.3-59.4)	Population-based controls and depressed patients from the BiDirect prospective cohort study	MINI modules A and A', IDS, HRSD, CES-D	FFQ, Diet score based on German nutritional recommendations	Patients with atypical depression had worse diet quality than control group or patients with melancholic depression; no association was found between depression severity and diet quality.	Age, sex, marital status, education, job status, smoking status, BMI, physical activity, comorbidities, antidepressant intake
Sinclair, 2016 (Fiji)	Baseline 7237 (52.6); follow-up 2948 (55.8)	Baseline 15.6 (1.4); follow-up 17.4 (0.9)	Fijian adolescents participating in the Healthy Youth Healthy Communities (HYHC) Study	PedsQLTM 4.0, emotional subscale	ABAKQ, Dietary patterns by factor analysis	Higher scores in emotional well-being scale were associated with healthy diet quality cross-sectionally in two time points (with highest healthy diet category, B = 7.9 and 5.0)	Age, ethnicity, condition, BMI, activity
Gibson-Smith et al., 2018 (Netherlands)	1634 (67.8)	52.0 (13.2)	Current depressive and anxiety disorder patients, remitted patients and healthy controls from the Netherlands Study of Depression and Anxiety	Diagnosis by CIDI, IDS-SR	FFQ, MDS, AHEI	Depression severity was associated with poorer diet quality (B = -0.11)	Age, sex, education, marital status, smoking, physical activity, energy intake
Errisuriz et al., 2019 (US)	534 (100)	40.7 (9.9)	Foreign-born Latina women living on the US-Mexico border	CES-D	Block FFQ, HEI	Depressed participants had significantly lower odds of having high-quality diet than non-depressed participants (OR 0.62).	Age, cohort, education, income, time spent in US, BMI, physical activity

Table 2: Research examining associations of depression with overall diet quality *(Continued)*

Author, year, country	n (% Women)	Mean age (±SD/range)	Population description	Depression assessment	Dietary assessment	Summary of associations	Adjusted for confounders
Elstgeest et al., 2019 (Netherlands)	Cross-sectional: 1312 (51.9) Change: 1233 (51.5) History: 687 (50.5)	65.1 [61.1–72.0]; 65.2 [61.2–71.9]; 71.2 [67.2–77.2]	Older adults from The Longitudinal Aging Study Amsterdam (LASA) cohort Nutrition and Food-related Behaviour side study; depression was measured at different time points in relation to diet assessment	CES-D	FFQ, MDS, AHEI, DASH	Chronic/recurrent depressive symptoms were associated with worse diet quality (B = -2.22); depressive symptoms were cross-sectionally associated with worse diet quality in men only (B = -1.21)	Age, sex, cohort, education level, marital status, physical activity, smoking, number of chronic diseases.
Paans et al., 2019 (Netherlands)	1442 (64.1)	51.7 (13.5)	Current depressive patients, remitted patients and healthy controls from the Netherlands Study of Depression and Anxiety	Diagnosis by CIDI, IDS-SR	FFQ, MDS	Depression diagnosis was associated with poorer diet quality (B = -1.11); depression severity was associated with poorer diet quality (B = 0.63)	Age, sex, years of education, marital status, smoking, physical activity and total energy intake
Matta et al., 2019 (France)	64 861 (54.0)	49.1 (12.4)	Participants from population-based Constances cohort study	CES-D	FFQ, Dietary patterns by principal components	Depressed individuals had lower odds of following a healthy diet (OR 0.78) and a higher odd of following unhealthy diet (OR 1.23)	Sex, age, education, household income
Jaalouk et al., 2019 (Lebanon)	457 (37.2)	21.3 (1.9)	Random sample of Lebanese private university students	PHQ-9	FFQ, Dietary patterns by factor analysis	No association was found between depression severity and diet quality	Age, sex, income, physical activity, BMI, family history of mental illness, alcohol consumption, stressful life events, worry of losing control over eating, antidepressant use

Abbreviations: *MDD* Major Depressive Disorder, *BDI-II* Beck Depression Inventory II, *HRSD* Hamilton Rating Scale for Depression, *AHEI* Alternate Healthy Eating Index, *BED* Binge Eating disorder, *BMI* Body Mass Index, *FFQ* Food Frequency Questionnaire, *MINI* Mini International Neuropsychiatric Interview, *IDS* Inventory of Depressive Symptomatology, *CES-D* The Center for Epidemiological Studies Depression Scale, *PedsQLTM 4.0* Pediatric Quality of Life Inventory 4.0 Generic Core Scales, *ABAKQ* Adolescent Behaviours, Attitudes and Knowledge Questionnaire, *CIDI* Composite International Diagnostic Interview, *IDS-SR* Inventory of Depressive Symptomatology - Self Report, *MDS* Mediterranean Diet Score, *HEI* Healthy Eating Index, *DASH* Dietary Approaches to Stop Hypertension score, *PHQ-9* The Patient Health Questionnaire 9

1.2 Depression and food choices

In addition to the studies examining the association between depression and overall diet quality, some research has focused on the association between food choices and single diet factors with depression. Depressive symptoms have been connected to a lower intake of vegetables and fruit in multiple studies (Konttinen et al., 2010; Cuy Castellanos, Connell & Lee, 2011; McMartin, Jacka & Colman, 2013; Grases, Colom, Sanchis & Grases, 2019; Errisuriz et al. 2019). In contrast, Appelhans et al. (2012) did not find a connection between fruit and vegetable consumption and depression. However, the sample of Appelhans et al. (2012) consisted only of obese women, whose diet may differ widely from that of the general population.

Depression has also been repeatedly associated with increased consumption of sweet and salty energy-dense snacks and fast food (Konttinen et al., 2010; Crawford, Khedkar, Flaws, Sorkin & Gallicchio, 2011; Grases et al., 2019; Paans et al., 2019). Despite the consumption of energy-dense foods, the studies that have reported total energy intake have not found association for depression diagnosis or depression severity with energy intake (Konttinen et al., 2010; Paans et al., 2019). This could be explained by loss of appetite, which is a common symptom of depression. However, depression has been associated with increased risk of weight gain and obesity (Blaine, 2008; Konttinen, van Strien, Männistö, Jousilahti & Haukkala, 2019). Since the estimates of energy intake are based on self-report, underreporting of food intake is possible, as it is common issue in nutrition research (Subar et al., 2015). Furthermore, physical inactivity associated with depression can also contribute to weight gain, as well as some medications for depression.

Although longitudinal evidence on depression's effects on overall diet quality is lacking, there are some studies that have examined the association of depression with specific diet characteristics longitudinally. In a 2013 study, those who had more depressive symptoms had more diet-related health-compromising behaviors at later time points (Walsh, Senn & Carey, 2013). Similarly, depression was positively associated with later unhealthy eating behaviors (consumption of foods with excess salt, sugar or fat) among school students followed for 10 years (Wu et al., 2016). In a recent study, depressive symptoms were associated with a decrease in consumption of vegetables and red/processed meat and increase in consumption of salty snacks and dairy products in 3-year intervals measured over a 9-year period (Elstgeest et al., 2019b). In contrast, emergence of depression did not associate with changes in energy, fiber, protein or saturated fat intake in one year follow-up of community-dwelling seniors (Gougeon et al., 2017).

When taking into account studies conducted so far on association of depression with both overall diet quality and separate food choices, it seems that depression is indeed connected to unhealthier eating behaviors. Thus, diet could play a part in preventing the undesirable consequences of depression on later-life health outcomes. Finding ways to influence effects of depression on diet quality is important, and dietary interventions could be a potential way to mitigate these associations.

1.3 Dietary interventions, lifestyle diseases and depression

In general population, dietary interventions have been researched in prevention of chronic diseases. A 2017 systematic review found that dietary counselling for adults in primary care settings resulted in improvement of at least one measure of dietary intake in most of the studies included (Mitchell, Ball, Ross, Barnes & Williams, 2017). However, some studies failed to achieve improvements in diet quality, and some failed to achieve improvements in central dietary characteristics such as energy or fat intake (Mitchell et al., 2017). Furthermore, even though dietary interventions appeared to be effective in weight loss and diabetic outcomes, there was no strong evidence to support their effectiveness in improving blood lipid levels or blood pressure (Mitchell et al., 2017). A 2013 Cochrane review reported that dietary advice for adults can result in improvement in cardiovascular risk factors as well as intake of fruit and vegetables, fiber and saturated fat; however, these improvements are typically modest (Rees et al., 2013). Similar results have been found among young adults studying at university/college (Plotnikoff et al., 2015). Since dietary behaviors take root in childhood, preventive interventions could potentially be more effective earlier in life. Furthermore, since lifestyle factors can have a cumulative effect on the risk of lifestyle diseases such as cardiovascular disease, childhood and youth are seen as an important period in the prevention of these diseases (Weintraub et al., 2011). In a 2012 meta-analysis, dietary interventions were found effective in weight loss among children and adolescents, as well as improvement of cardiometabolic risk factors (Ho et al., 2012). In Finland, a population-based early-onset preventative dietary intervention has been associated with favorable outcomes in diet quality sustaining from childhood to young adulthood (Matthews et al., 2019). The same intervention has also resulted in favorable outcomes in cardiometabolic factors, such as LDL cholesterol and risk of metabolic syndrome (Niinikoski et al., 2012; Nupponen et al., 2015).

Dietary interventions may have potential in improving diet quality and risk factors for chronic disease, especially if they are started early in life. Thus, it is important to consider if they could mitigate the effects of depression on diet. However, there is not much research on the associations of preventative dietary interventions and depression. There is some evidence that depressive symptoms can have a negative effect on adherence to and results of dietary interventions (Somerset, Graham & Markwell, 2011; Cezaretto et al., 2015; Wang et al., 2015). However, in two randomized controlled trials that investigated if dietary intervention could be effective in reducing depressive symptoms, patients with depression did improve their diet quality (Jacka et al., 2017; Parletta et al., 2017). In first of these studies, a 12 week dietary intervention conducted by a nutritionist and based on Australian dietary recommendations resulted in improved diet quality compared to both baseline and control group (Jacka et al., 2017). In the second study, a 3 month intensive Mediterranean diet intervention resulted in greater improvements in diet quality compared to control group, and the results were sustained 3 months after the end of intervention (Parletta et al., 2017). Effectiveness of dietary interventions has also been researched among people with severe mental illness. A pilot study found Mediterranean diet intervention to result in qualitative improvements in diet quality of patients with severe mental illness; however, small sample size limits the interpretation of these results (Bogomolova et al., 2018). On the contrary, in another study with patients with severe mental illness, a multifaceted lifestyle intervention including dietary guidance did not result in improvements in diet quality measured with fiber, fat and saturated fat intake (Osborn et al., 2018). In this study, the dietary intervention was not conducted by a nutritionist, and measures of overall diet quality were not reported.

Based on previous research, dietary interventions seem promising in improving diet quality in people with depression (Jacka et al., 2017; Parletta et al., 2017). However, these interventions have been relatively short and they have been conducted on people with depression reported prior to the intervention. Therefore, these studies do not bring information about preventative effects of dietary interventions in context of depression. Since the follow-up times of these studies have also been short, it is not known if the results persist over longer time periods. Research of preventative dietary interventions is needed to investigate if they would mitigate the association between depression and diet. Since childhood and youth represent important era in prevention of

later-life negative health outcomes, early-onset interventions should be examined in context of depression and diet.

1.4 Research questions and hypotheses

Prior research indicates that depressive symptoms could be a risk factor for unhealthy diet. Depression is also a common disorder in western societies and therefore influences public health both directly and potentially through lifestyle factors. Since prevention of chronic diseases is most effective in young people, it is important to investigate how depressive symptoms affect eating behavior in this age group. Prior research on the topic is focused on cross-sectional correlations between current depression and diet, thus it is important to learn more about longitudinal effects of depressive symptoms on diet. In this study, data from a Finnish longitudinal population-based preventive intervention study, the Special Turku Intervention Project (STRIP), is used to analyze the association of depressive symptoms with diet quality at two time points in Finnish young adults. In addition, the aim of this study is also to investigate if dietary intervention of the STRIP project affects these associations. Research questions are follows: 1) Is there a cross-sectional association of depressive symptoms with diet quality at the age of 20 years? 2) Is there a longitudinal association of depressive symptoms at the age of 20 with diet quality at the age of 26 when adjusting for diet quality at the age of 20? 3) Does a long-term preventive dietary intervention modify the association between depressive symptoms and diet quality?

It is hypothesized that depressive symptoms at the age of 20 would be associated with worse diet quality at the same age, and also at age 26. It is also hypothesized that the association of depression with worse diet quality will be mitigated by the preventive dietary intervention of the STRIP project.

2 Methods

2.1 Study design and participants

The Special Turku Coronary Risk Factor Intervention Project (STRIP) investigates the effects of an early-onset preventative dietary intervention on dietary habits and risk of heart disease (Simell et al., 2009). Families from Turku area in Finland were recruited in 1990 during routine five-month-

old well-baby clinic visits. Total of 1062 infants were randomized into intervention (n = 540) and control (n = 522) groups at the age of 7 months. The intervention group received dietary counselling until the age of 20 years, while the control group received standard guidance provided by the Finnish health care system. Both of the groups were prospectively followed from 7 months until 20 years of age, intervention group at least biannually and control group at least annually. There was also a follow-up at the age of 26 for both of the groups.

The intervention group attended 30-minute dietary counselling sessions led by a nutritionist. The sessions were carried out at 1-3 month intervals from the age of 7 months until the age of 2 years and biannually thereafter until the age of 20. No fixed diet was suggested, instead, the sessions were individualized based on the participant's recent food record. The dietary recommendations were based on the most recent Nordic Nutrition Recommendations available at the time (e.g., 30 percent of energy intake E% from fat, 10–15 E% from protein, and 50–60 E% from carbohydrates). The main goal was to reduce saturated fat intake in diet and secondary goals were to reduce salt and cholesterol intake, favor unsaturated fats instead of saturated fats and increase the consumption of vegetables, fruits and whole grains. Reasonable portion sizes were also promoted. At the beginning, the counselling was targeted primarily to the parents. From the age of 7, the counselling was increasingly targeted to the participants themselves depending on their reading skills and maturity level. The control group received only the standard dietary guidance given by Finnish school and health care systems.

For the current study, information from follow-ups at the ages of 20 and 26 was used to assess diet quality and number of depressive symptoms. Total of 457 subjects (43 % of the original sample) participated in the follow-ups at the ages of 20 and 26, of whom 209 (46 %) were part of the intervention group and 248 (54 %) were part of the control group.

2.2 Measurements

Diet quality

For the current study, diet quality was assessed at the ages of 20 and 26. Participants from both groups completed a 4-day food record before each study visit. The food records were instructed to consist of four consecutive regular days (not i.e. sick days or holidays) including at least one weekend day, and they were instructed to contain detailed information about the foods (e.g.

brand and preparation). The food quantities were estimated using common Finnish household measurements or weight, and a booklet with visualizations of food portion sizes was sent along with the instructions to help with the estimation of quantities. The completeness and accuracy of the food records was reviewed by a nutritionist, and possible missing information was added based on interviewing. When needed, further information was also gathered from restaurants and manufacturers. Data from the food records was entered into the Micro-Nutrica[®] food analysis software (Research Center of the Social Insurance Institution, Turku, Finland), and food and nutrient intakes were calculated.

A food-based diet score was created following a multi-cohort study by Nettleton et al. (2013) and a study by Matthews et al. (2019) in this same dataset. Eleven food groups were formed based on the evidence-based conclusions of the 2012 Nordic Nutrition Recommendations and the 2015-2020 Dietary Guidelines for Americans (Nordic Council of Ministers, 2014; US Department of Health and Human Services and US Department of Agriculture, 2015). Seven of the food groups were labelled as “favorable” as they are found to associate with lower risk of chronic disease (e.g. vegetables and whole grains). Four food groups were labelled as “unfavorable” since their associations with higher chronic disease risk (e.g. red and processed meat). Food groups are presented in Table 2.

Daily intake of foods and beverages was calculated as grams per energy intake. Intake of different foods was then classified based on quartiles of consumption. Foods from favorable groups were given ascending values (0,1,2,3), and foods from unfavorable groups were given descending values (3,2,1,0). An overall diet score was created as a sum of values from each food group. The diet score ranged from 0-33, where higher scores indicated healthier diet consisting of high intake of favorable foods and low intake of unfavorable foods.

Depression

Depressive symptoms were assessed at the age of 20 with the Beck Depression Inventory II (BDI-II) (Beck, Steer & Brown, 1996). BDI-II is a widely used multiple-choice self-report questionnaire consisting of 21 items that ask about different depressive symptoms, for example ‘I have lost interest in everything’ and ‘I am too tired to do things I should do’ (Beck et al., 1996). Responses to each item are given on a four-point scale, with higher scores indicating more severe symptoms. Sum of item responses was calculated to assess the total number of depressive symptoms.

Table 3. Food groups used in calculations of the diet score. Adapted from Matthews et al. (2019).

Food group	Description
Favorable food groups	
Fiber-rich grain products	Bread, flour and flakes with fiber content $\geq 5\text{g} / 100\text{g}$. Excluding snacks, biscuits, cereals, muesli and snack bars.
Vegetables	Fresh and frozen edible roots, corn, pulses and sprouts. Excluding potatoes, mushrooms, preserves, soups and soy products.
Fish	Fresh, smoked and canned fish, shrimp, crab and crayfish. Excluding roe, mussels, squid and salted fish.
Nuts and seeds ¹	Excluding salted, sugar coated or flavored nuts/seeds.
Low-fat dairy	Milk, fermented milk, quark and fermented curdled milk with $\leq 1\%$ fat, cottage cheese and vegetable fat cheese with $\leq 17\%$ fat. Excluding creams and flavored and sweetened dairy products.
Vegetable oil fats	Oils, margarines, flavored oils and salad dressings. Excluding mayonnaises and baking margarines.
Unfavorable food groups	
Red and processed meat	Pork, beef and sheep meat, sausages, pates and cold cuts.
Sugary drinks	Juices, soft drinks and energy drinks with sugar $\geq 0.6\text{g} / 100\text{ml}$. Excluding alcoholic beverages, natural fruit juices, protein shakes and sports drinks.
Salty snacks ²	Potato chips, salted nuts, popcorn, cheese-flavored corn snacks.
Sweet snacks	Puddings, ice cream, chocolate, cocoa drink powder, sugar.

Favorable food groups: Range from 0 to 3, scored conversely by quartile

Unfavorable food groups: Range from 0 to 3, scored inversely by quartile

¹Since consumption was low in previous studies, scoring was dichotomized: any consumption scored 3, no consumption scored 0

²Since consumption was low in previous studies, scoring was dichotomized: any consumption scored 0, no consumption scored 3

Background variables

Educational level was assessed at the age of 20. Participants filled a background information form including the question “What is the highest educational level you have reached or that you are currently attending to?”. The responses were categorized as follows: 1) Primary school, 2) Upper

secondary school (Finnish matriculation examination or vocational upper secondary qualification), 3) University of applied sciences degree and 4) University degree. Sex was recorded as a part of the data collection.

2.3 Statistical analyses

Linear regression analyses were used to investigate the associations between diet and depression. First, separate linear regressions were calculated using depression at age 20 as independent variable, and diet quality at ages 20 and 26 as dependent variables. These analyses were then adjusted for sex and educational level. The analysis on the association of diet at the age of 26 with depression was additionally adjusted for diet at age 20 in order to examine the contribution of depressive symptoms on the residual of diet, that is, on the part not explained by diet in the previous time point.

To examine the potential modifying effect of dietary intervention on the association of depression with diet, regression analyses stratified by intervention group were calculated using depression at age 20 as independent variable and diet quality at ages 20 and 26 as dependent variables. Stratified analyses were adjusted for sex and educational level, and the analysis for diet at age 26 was additionally adjusted for diet at age 20. Finally, the adjusted regression analyses for the whole sample were repeated with interaction effect for intervention group and depression included.

Multiple imputation by chained equations

The data contained considerable amount of missing values, especially in the diet score variables. Distribution of missing values in the diet score variables in association with other analyzed variables was analyzed using chi-squared test for categorical variables and Kruskal Wallis test for continuous variables. The R package “finalfit” was used for the analyses (Harrison, Drake & Ots, 2020). Multiple imputation by chained equations (MICE) was used to impute the missing values in order to achieve better statistical power and avoid potential bias in analyses resulting from non-random missingness. MICE creates a set of imputation models, one for each variable with missing values (White, Royston & Wood, 2010). Imputation process starts with replacement of missing values in each variable by random observed values. The first variable with missing values (x_1) is regressed on every other variable in the imputation model (x_2, \dots, x_k) using those individuals that have the observed value in x_1 . This results a posterior predictive distribution of x_1 , which is then

used to simulate values to replace missing values in x_1 . Next, the process is repeated for x_2 using variables x_1, x_3, \dots, x_k for regressions, and then for all other variables with missing values. Once all variables with missing values have been regressed against all the other variables, a cycle is complete. The cycle is repeated multiple times to create multiple imputed datasets, which stabilizes the random error caused by the use of random observed values in estimation of the regression models (White et al., 2010).

In this study, MICE was performed using predictive mean matching to create 50 imputed datasets. Since it was assumed that missing values in the diet score variables were not completely random, additional variables were used in the imputation model along with the variables of interest in order to increase its reliability (White et al., 2010). Final model consisted of following variables: BDI-II score, diet scores at both age points, sex, education, group (intervention/control), time of unemployment, financial difficulties, amount of stress, amount of social support and negative affectivity. R package “MICE” was used for calculations (van Buuren & Groothuis-Oudshoorn, 2011). Pooled regression analyses were calculated using the imputed datasets. As a sensitivity analysis, regression analyses were repeated among the 155 individuals in the original dataset that had no missing values in any of the variables of interest. All analyses were performed using R version 3.6.1 (R Core Team, 2017).

3 Results

Results for missing values analysis are presented in Table 3. Those who had missing values in diet score variables in either of the time points had higher depression scores on average at age 20 (Appendix 1). In addition, those who had missing values on the diet score variables in either time point were less educated and more often belonged to the intervention group. At age 26, those with missing values on the diet score variables were more often men.

Descriptive characteristics of the participants after multiple imputation are presented in Table 4. Depression scores at age 20 ranged from 0 to 44 with the mean of 7.20 (SD 7.62), which is well below the cut-off score 13 for mild depression. Diet scores ranged from 4 to 32 with the mean of 16.45 (SD 4.76) at age 20, and from 3 to 32 with the mean of 18.20 (SD 5.02) at age 26.

Characteristics of the participants in the complete cases data where missing values were excluded

are presented in Appendix 2. There were no considerable differences in characteristics between the imputed and complete cases data sets.

Table 3. Distribution of missing values in diet score variables in association with depression, gender, educational level and group.

		Diet at age 20			Diet at age 26		
		Not missing	Missing	p	Not missing	Missing	p
Depression							
Mean (SD)		5.7 (6.2)	8.7 (8.5)	<0.001	6.5 (6.9)	8.3 (8.5)	0.02
Gender							
Freq. (%)	Female	145 (65.0)	137 (59.1)	0.22	178 (66.4)	104 (55.6)	0.03
	Male	78 (35.0)	95 (40.9)		90 (33.6)	83 (44.4)	
Education							
Freq. (%)	1 (Basic education)	2 (0.9)	12 (5.2)	0.02	4 (1.5)	10 (5.3)	0.01
	2 (Upper secondary)	103 (46.4)	104 (44.6)		112 (42.1)	95 (50.3)	
	3 (University of appl. sc.)	53(23.9)	40 (17.2)		66 (24.8)	27 (14.3)	
	4 (University)	64 (28.8)	77 (33.0)		84 (36.1)	57 (30.2)	
Group							
Freq. (%)	Intervention	88 (39.3)	121 (51.9)	0.01	112 (41.8)	97 (51.3)	0.06
	Control	136 (60.7)	112 (48.1)		156 (58.2)	92 (48.7)	

Table 4. Descriptive characteristics of the data after multiple imputation

Variable	
Sex, n (%)	
Female	282 (62)
Male	175 (38)
Education, n (%)	
Education level 1 (Basic education)	14 (3)
Education level 2 (Upper secondary)	208 (49)
Education level 3 (University of applied sc.)	94 (19)
Education level 4 (University)	141 (29)
Diet score at 20, mean (SD) ¹	16.45 (4.76)
Diet score at 26, mean (SD) ¹	18.20 (5.02)
Depression: BDI-II score, mean (SD) ²	7.20 (7.62)

¹ Maximum value for diet score was 33

² Maximum value for BDI-II score is 63 and cut-off for mild depression is 13

3.1 Associations of depression with diet

Results from linear regression analyses after multiple imputation are presented in Tables 5 and 6. In unadjusted analysis, depression score at age 20 was not associated with diet quality at age 20 ($B = -0.01$, 95% CI $-0.11; 0.09$, $p = .83$). The association remained non-significant after adjusting for sex and educational level ($B = -0.01$, 95% CI $-0.11; 0.09$, $p = .68$) (Table 5).

Table 4. Results from linear regression analyses predicting diet quality at age 20 with depressive symptoms at age 20.

	Model 1		Model 2	
	B	95 % CI	B	95 % CI
Depression	-0.01	-0.11; 0.09	-0.01	-0.11; 0.09
Sex (Female)			1.31*	0.04; 2.58
Education 2 (Upper secondary)			-1.73	-5.95; 2.50
Education 3 (University of applied sc.)			0.20	-4.17; 4.58
Education 4 (University)			0.47	-4.04; 4.98
R ²	0.003		0.08	

For gender, male gender was used as a reference. For education, lowest educational level (basic education) was used as a reference.

Model 1: Unadjusted. Model 2: Adjusted for sex and educational level.

* $p < .05$, ** $p < .01$, *** $p < .001$

Higher depression score at age 20 was associated with worse diet quality at age 26 ($B = -0.09$, 95% CI $-0.16; -0.01$, $p = .03$). The association remained significant after adjusting for sex and educational level ($B = -0.08$, 95% CI $-0.16; -0.01$, $p = .03$), and also after additionally adjusting for diet at age 20 ($B = -0.08$, 95% CI $-0.15; -0.01$, $p = .04$) (Table 4).

Table 5. Results from linear regression analyses predicting diet quality at age 26 with depressive symptoms at age 20.

	Model 1		Model 2		Model 3	
	B	95 % CI	B	95 % CI	B	95 % CI
Depression	-0.09*	-0.16; -0.01	-0.08*	-0.16; -0.07	-0.08*	-0.15; -0.01
Gender (Female)			2.08**	0.80; 3.35	1.83**	0.56; 3.09
Education 2 (Upper secondary)			1.19	-2.53; 4.91	1.53	-2.07; 5.14
Education 3 (University of applied sc.)			2.22	-1.52; 5.96	-1.58	-1.43; 5.82
Education 4 (University)			3.86*	0.10; 7.62	3.78*	0.11; 7.44
Diet at the age of 20					0.19*	0.05; 0.34
R ²	0.02		0.13		0.16	

For gender, male gender was used as a reference. For education, lowest educational level (basic education) was used as a reference.

Model 1: Unadjusted. Model 2: Adjusted for sex and educational level. Model 3: Additionally adjusted for diet at age 20.

* $p < .05$, ** $p < .01$, *** $p < .001$

3.2 Modifying effects of intervention

In the stratified analyses for depression at age 20 and diet quality at age 20, the associations did not differ for intervention ($B = -0.01$, 95 % CI -0.14; 0.13, $p = .93$) and control ($B = -0.01$, 95 % CI -0.12; 0.10, $p = .83$) groups, and no interaction effect was found (for interaction, $B = -0.01$, 95% CI -0.15; 0.14, $p = .94$) (Table 7). Similarly, in the stratified analyses for depression at age 20 and diet quality at age 26, the associations were similar for intervention ($B = -0.10$, 95 % CI -0.21; 0.01, $p = .64$) and control ($B = -0.06$, 95 % CI -0.16; 0.03, $p = .19$) groups, and no interaction effect was found (for interaction, $B = -0.04$, 95% CI -0.18; 0.01, $p = .57$) (Table 8). The models were adjusted for sex and educational level, and the longitudinal model was also adjusted for diet at age 20.

Table 7. Results from group stratified regression analyses predicting diet quality at age 20 with depressive symptoms at age 20.

	Intervention (n = 209)		Control (n = 248)	
	B	95 % CI	B	95 % CI
Depression	-0.01	-0.14; 0.13	-0.01	-0.12; 0.10
Sex (Female)	0.82	-0.02; 2.66	1.67	0.10; 3.24*
Education 2 (Upper secondary)	-1.75	-7.08; 3.59	-1.36	-6.81; 4.10
Education 3 (University of applied sc.)	0.51	-4.86; 5.89	0.03	-5.85; 5.90
Education 4 (University)	0.61	-4.91; 6.13	0.38	-5.50; 6.53
R ²	0.08		0.09	

For gender, male gender was used as a reference. For education, lowest educational level (basic education) was used as a reference.

* $p < .05$, ** $p < .01$, *** $p < .001$

Table 8. Results from group stratified regression analyses predicting diet quality at age 26 with depressive symptoms at age 20.

	Intervention (n = 209)		Control (n = 248)	
	B	95 % CI	B	95 % CI
Depression	-0.10	-0.21; 0.01	-0.06	-0.16; 0.03
Sex (Female)	0.98	-0.85; 2.81	2.42	0.80; 4.04**
Education 2 (Upper secondary)	2.11	-2.46; 6.67	1.17	-4.00; 6.34
Education 3 (University of applied sc.)	2.30	-2.23; 6.82	2.03	-3.17; 7.23
Education 4 (University)	3.47	-1.03; 7.78	3.84	-1.56; 9.25
Diet at age 20	0.16	-0.02; 0.35	0.19	-0.02; 0.39
R ²	0.13		0.19	

For gender, male gender was used as a reference. For education, lowest educational level (basic education) was used as a reference.

* $p < .05$, ** $p < .01$, *** $p < .001$

3.3 Complete cases analyses

The results from linear regression analyses in the complete cases sample are shown in Appendix 3. No significant associations were found for depression score at age 20 with diet quality neither at age 20 or 26 in complete cases data. Similarly to the analyses after multiple imputation, no interaction effects were found between the number of depressive symptoms and intervention group in the complete cases data.

4 Discussion

In this study, data from a longitudinal population-based preventive intervention project (STRIP) was used to investigate associations of depressive symptoms with diet, and contribution of early-onset dietary intervention to these associations. No cross-sectional association was found for depressive symptoms with diet quality at the age of 20. However, a higher level of depressive symptoms at the age of 20 was longitudinally associated with worse diet quality at age 26 when controlling for diet at age 20. Contrary to the hypothesis, there was no mitigating effect by the dietary intervention, as the associations between depressive symptoms and diet quality did not differ between intervention and control groups at either of the time points.

4.1 Findings on the association of depression with diet

In previous research, depression has been found to be associated with worse diet quality. Cross-sectionally, high number of depressive symptoms has been linearly associated with worse diet quality (Appelhans et al., 2012; Sinclair, 2016; Gibson-Smith et al., 2018; Paans et al., 2019). Compared to people with no depression, people with depression have been less likely to have healthy diets (Jacka et al., 2015; Errisuriz et al., 2019; Paans et al., 2019; Matta et al., 2019). In contrast to previous studies, the present study did not find a cross-sectional association for depression and diet. While most previous studies have included middle-aged adults (Appelhans et al., 2012; Rahe et al., 2015; Gibson-Smith et al., 2018; Errisuriz et al., 2019; Paans et al., 2019; Matta et al., 2019), the present study was conducted at the age of 20 years. One potential explanation for the null findings could thus be a difficulty to observe an association at this specific age, as some evidence suggests that a shift to unhealthier dietary behaviors occurs on average in

early adulthood (Nelson et al., 2008). In line with this possibility, one previous study that investigated depression and diet quality among students in their early 20's also failed to find an association (Jaalouk et al., 2019).

Furthermore, the current study was conducted in a population-based sample that typically comprises individuals with little to none depressive symptoms. This may lead to difficulties in observing linear associations, as the whole spectrum of depression severity is not equally represented. In some previous studies, the samples consisted of clinically depressed participants (Appelhans et al., 2012) or had a subsample of depressive patients (Rahe et al., 2015; Gibson-Smith et al., 2018; Paans et al., 2019). Association of depression with diet quality could thus be more easily observed in these types of samples. Some population-based studies have also been able to compare depressed participants with non-depressed participants, and have found a difference between these groups (Jacka et al., 2015; Errisuriz et al., 2019; Matta et al., 2019). In the sample of this study, there were only few individuals that had a depression score over the lowest cut-off point for mild depression, suggesting that most of the participants were free from any depressiveness. This made comparisons between depressed and non-depressed individuals unreasonable.

It is also possible that the large amount of missing values in the data affected the results even after multiple imputation. There was even more missing data in the diet score at age 20 compared to age 26, and the distribution of missing values was very skewed in terms of depression (Appendix 1). Only few of those who had higher depression scores at age 20 had an observed value on diet score at age 20. Imputing non-random missing values can cause error that may bias the observed linear associations, especially when there are large amounts of missing values and some of them reach beyond the range of observed values (White et al., 2010; van Buuren & Groothuis-Oudshoorn, 2011). However, multiple variables were used in the imputation models in this study, alongside with a reasonably large amount of imputed datasets and predictive mean matching as a method. These measures should minimize bias in imputation (White et al., 2010).

No previous research has focused on longitudinal associations of depression with overall diet quality. However, in some previous studies, depressive symptoms have longitudinally predicted some unhealthy eating behaviors, such as increases in salty snack consumption over time (Walsh et al., 2013; Wu et al., 2016; Elstgeest et al., 2019b). In this study, depressive symptoms measured at the age of 20 predicted worse diet quality six years later. This finding is in line with previous

research on supporting the association of depression with diet, as well as previous findings that depression may lead to unhealthy eating habits over time. The finding suggests that depressive symptoms can have negative effects on diet quality that reach beyond the current moment and might manifest themselves for at least several years. Although the association of depression with diet was significant, it was not very strong. This has been the case in most of the cross-sectional studies that have reported association between depression and diet quality (Appelhans et al., 2012; Jacka et al., 2015; Gibson-Smith et al., 2018; Elstgeest et al., 2019a; Paans et al., 2019). It must however be noted that even small effects can be relevant at the population level, especially if they extend over long periods of time.

4.1.1 Explanations for the association of depression with diet

Different mechanisms have been proposed on how depression can affect dietary behaviors. It was suggested already over two decades ago, that depression can lead to craving of high-carbohydrate foods due to inadequate serotonin levels in the brain (Wurtman & Wurtman, 1995). Foods that are high in carbohydrates and low in protein increase blood insulin levels, which enables more serotonin precursor tryptophan to access the brain (Wurtman & Wurtman, 1995). Thus, high-carbohydrate foods can have temporal positive effects on mood by modifying serotonin levels. Foods that are high in carbohydrates are often also rich in fat or/and salt, and their regular consumption has negative effects on overall diet quality. Hypothesis on serotonin's effects on food cravings is supported by evidence indicating that serotonin reuptake inhibitor fluoxetine may aid weight loss and prevent post smoking cessation weight gain (Domecq et al., 2015; Serralde-Zúñiga, Gonzalez Garay, Rodríguez-Carmona & Melendez, 2019; Farley, Hajek, Lycett & Aveyard, 2012).

Palatable foods have also potential in relieving psychological distress by decreasing HPA-axis activity (Adam & Epel, 2007). Depression is associated with abnormal HPA-axis activity, and eating palatable foods can thus bring temporal relief for people with depressive symptoms (Zunszain, Anacker, Cattaneo, Carvalho & Pariante, 2011). Furthermore, psychological stress has been suggested to increase appetite and rewarding effects of high-calorie foods via glucocorticoid signalling (Adam & Epel, 2007). Psychological stress can also influence motivational and executive brain responses towards high-calorie foods, leading to sensitivity for palatable food cues (Tryon, Carter, DeCant & Laugero, 2013). In line with this, it has been observed that depression is associated with external eating style, i.e. increased sensitivity towards external food cues (Sevinçer et al., 2016; van Strien et al., 2016). Thus, people with depression might be more

susceptible to respond to high-calorie food cues in the environment, and have less executive control to make food choices that are beneficial in the long run. Depression has also been associated with the so-called emotional eating style (Evers et al., 2010; Konttinen et al., 2010; van Strien et al., 2016; Konttinen et al., 2019). Emotional eating is described as a tendency to eat palatable energy-dense foods in response to negative emotions (Konttinen et al., 2019). In other words, food can be used as a maladaptive emotion regulation strategy among people with depression. Constant use of food for emotion regulation could affect overall diet quality if healthy foods are replaced with high-energy comfort foods. Emotional eating has also been observed to mediate effect of depression on weight gain over a 7-year period (Konttinen et al., 2019). Thus, emotional eating could be one potential explanation for depression's longitudinal associations with diet quality. So far, one study has examined if emotional eating mediates the association of depression with poor diet quality (Paans et al., 2019). In this study, depression and emotional eating were independently associated with poor diet quality, and no mediating effects were found (Paans et al., 2019).

Although mechanisms to explain how depression might affect diet quality have been suggested, their role in the association of depression with diet has not been extensively researched. Better understanding of these mechanisms would be beneficial when considering ways to influence the association of depression with diet quality.

4.2 Efficacy of dietary intervention in modifying the association of depression with diet

Another aim of this study was to see if early-onset preventive dietary intervention could reduce the adverse effects of depressive symptoms on diet quality. The participants of the intervention group had undergone dietary intervention that started when the subjects were seven months old and continued until the age of 20. The intervention of the STRIP project has previously been found effective in improving diet quality of the intervention group in general (Matthews et al., 2019).

Contrary to hypothesized, there were no differences between intervention and control groups in association of depression at age 20 with diet quality at either age of 20 or 26. This is in contrast with two previous randomized controlled trials that examined the efficacy of dietary interventions in improving depressive symptoms, and found that the dietary interventions did indeed lead to improvement in diet quality (Jacka et al., 2017; Parletta et al., 2017). In these studies, the

interventions were relatively short (3 months) and intensive, and study participants were clinically depressed prior to the intervention. Thus, the setting differs from that of the present study, where dietary intervention was long and preventive in nature. In addition to interventions of these previous studies being short, the follow-up times were not long: the span of the 3 month intervention in one (Jacka et al., 2017) and 6 months in the other (Parletta et al., 2017). Because of the short follow-up times, it is not known if the dietary improvements achieved in these studies last over time. Furthermore, there is a possibility for selection bias in these previous studies, as participants have been at least partly aware of the purpose of the studies in the recruitment phase (Molendijk, Fried & van der Does, 2018). This could bias the observed efficacy of these interventions, if the participants have been more motivated to dietary changes than depressed people in general.

A recent study examining efficacy of a 6-month lifestyle intervention in patients with severe mental illness did not find improvement in diet quality or other lifestyle factors at the end of the intervention or at 12 months (Osborn et al., 2018). Although this could be due to inefficacy for this specific multifaceted intervention to address diet effectively, the result indicates that mental health issues may form an obstacle for the effectiveness of dietary intervention. The sample of this study consisted of patients with schizophrenia, psychosis or bipolar disorder (Osborn et al., 2018). Thus, it is uncertain if the results are generalizable among people with unipolar depression. However, it has been observed that depressive symptoms may impact adherence to dietary interventions (Somerset et al., 2011; Cezaretto et al., 2015; Wang et al., 2015). When considering these results and the result of the current study, it seems possible that dietary interventions might not be effective in mitigating the effects of depression on diet quality. However, as mentioned above, the population-based sample of this study had very limited amount of individuals with depressive symptoms even at the level of mild depression. It is possible that the effects of dietary interventions are easier to observe among those with more severe depressive symptoms. This could explain the difference in outcome of this study and the two previous trials that have found dietary intervention effective in improving diet quality of depressed people in clinical samples (Jacka et al., 2017; Parletta et al., 2017).

4.3 Limitations and strengths

As discussed above, the major weakness in this study was the large amount of missing data in the diet score variables. This may have biased the results even after multiple imputation, especially since there were large amounts of missing values within those subjects who had the highest scores on depression inventory. Since the data were from a population-based sample, the amount of subjects with higher depression scores was low to begin with, and thus the whole spectrum of severity of depressive symptoms was not equally represented in this study. Furthermore, due to the prospective nature of the study, natural loss to follow-up has occurred. Although there were no data available to assess if loss to follow-up was associated with depressive symptoms, several depressive symptoms, such as fatigue, lack of motivation and diminished interest, could potentially affect adherence to the study follow-ups. In such case, selective loss to follow-up could bias the results.

This study provided novel information on the longitudinal association of depression with diet quality, indicating that depression can have negative effects on diet quality that may manifest for several years. However, the results of longitudinal effects of depression on diet quality are based on observational data. Thus, direction of causality cannot be established from this study. Although the results give support to the idea that depression affects diet quality, it is also possible that the perceived associations are due to the effects of unhealthy diet on mood that could also manifest over longer periods of time. This direction of causality has been suggested in the literature before (Li et al., 2017; Molendijk et al., 2018; Nicolaou et al., 2019). Furthermore, the results of this study do not rule out the possibility that depression and diet affect each other in a reciprocal manner. This could lead to a vicious circle and have long term effects on dietary behaviors. Thus, the reciprocal relationship between depression and diet is potentially of public health relevance and needs to be explored further.

There were also strengths in this study. The data were from a longitudinal randomized controlled trial, providing a possibility to assess the modifying effect of dietary intervention on outcomes. Furthermore, randomized controlled trials lasting over decades are rare, the STRIP project being the longest dietary intervention conducted worldwide. Thus, this study provides unique information about the effects of a 20-year preventive dietary intervention on associations of depression with diet. Also, although there has been loss to follow-up during the trial, the attrition rate is acceptable for a prospective study this long. The sample size has decreased from original

1062 to 457, meaning that 43 % of the original study sample has attended to follow-ups after over 20 years. The sample size was also relatively high for an intervention study. As the original sample was gathered from a whole age group in a large Finnish city, the current study sample can be considered as a fairly good representation of Finnish young adults.

Another considerable strength was the diet quality assessment, which was conducted carefully in the STRIP project. Self-reported dietary information such as food diaries and food frequency questionnaires have typically several weaknesses, such as under- or overreporting of certain food groups or difficulties in remembering all the foods consumed (Subar et al., 2015; Garcia-Perez et al., 2017). Although these problems were probably not completely avoided in this study, the assessment of the food records and complementary interviews conducted by a nutritionist add to the reliability of a simple home-sent food diary or food frequency questionnaire. The participants were also well trained in documenting their food consumption, since follow-ups of their diet quality had been a part of their lives since early childhood.

4.4 Directions for future research

This study provided preliminary evidence that depression could have a negative impact on diet quality that can manifest even after several years. In future, more longitudinal research is needed to explore the association of depression with diet over time. In this study, the longitudinal association was found to extend for a 6-year period. Information from even longer follow-up periods would be needed to better understand how far the impact of depression on diet can extend. Since most of the previous research has been conducted with middle-aged adults in Western countries, longitudinal association of depression with diet should be researched in different populations and developmental stages. More longitudinal research could also lead to a better understanding of directions of causality in the depression-diet relationship. Mechanisms in which depression could affect diet quality have been suggested (e.g. Wurtman & Wurtman, 1995; Adam & Epel, 2007; Konttinen et al., 2010), but their role in explaining the association is unclear. In future, these mechanisms should be explored further.

A better understanding of mechanisms underlying the association of depression with diet could also lead to a better understanding of ways to influence diet among people with depression. Especially as it appears that depression might affect diet quality after several years, it is important

to explore ways to mitigate these effects in order to reduce negative health effects. In this study, preventive dietary intervention did not appear effective in mitigating the association. However, since there were some limitations in this study, the role of preventive interventions should be investigated more. There is some previous research suggesting that dietary interventions can be effective in improving diet quality among clinically depressed people (Jacka et al., 2017; Parletta et al., 2017). More studies including people with different degrees of depressive symptoms are needed to understand the effectiveness of dietary interventions better. Finally, as depression is associated with poor physical health (Scott et al., 2016), the role of dietary behaviors in explaining this association should be researched further.

4.5 Conclusions

This study provided novel information on longitudinal associations of depression with diet quality. Although no cross-sectional association between depression and diet measured at the same time point was found, depression appeared to have negative effects on diet quality that manifested after several years. In this study, a long-lasting early-onset preventive dietary intervention did not seem effective in mitigating depression's effect on diet quality. However, due to limitations in this study, more research on the efficacy of dietary interventions among depressed individuals is needed. Depression is associated with adverse physical health outcomes, and its long-term effects on diet could potentially be an important factor in explaining this association. More research is needed to assess this potential pathway.

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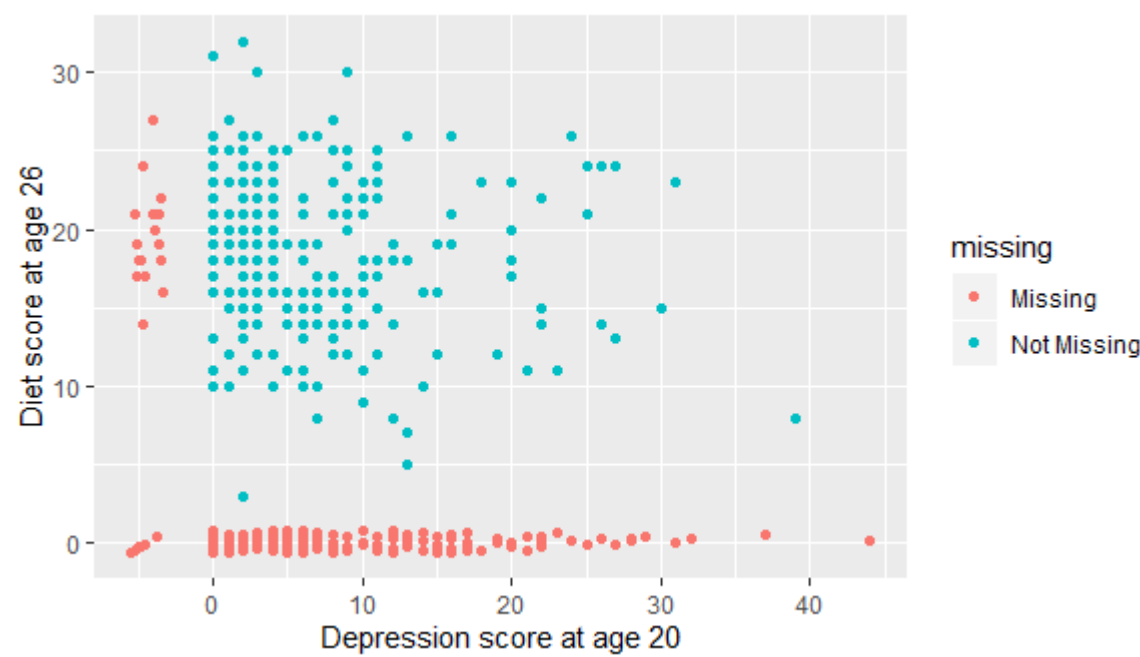
Appendix

1 Visualizations of missing values in diet scores according to depression

a) Missing values on diet score at age 20 and depression at age 20



b) Missing values on diet score at age 26 and depression at age 20



2 Descriptive characteristics of the complete cases data (n = 155)

Variable	
Sex, n (%)	
Female	106 (68)
Male	49 (32)
Education, n (%)	
Education level 1 (Basic education)	2 (<1)
Education level 2 (Upper secondary)	69 (45)
Education level 3 (University of applied sc.)	42 (27)
Education level 4 (University)	42 (27)
Diet score at 20, mean (SD)	16.21 (4.87)
Diet score at 26, mean (SD)	17.99 (5.24)
Depression: BDI-II score, mean (SD)	6.27 (6.72)

3 Results for linear regression analyses on complete cases data (n = 155)

a) Predicting diet quality at age 20 with depressive symptoms at age 20

	Model 1		Model 2	
	B	95 % CI	B	95 % CI
Depression	0.01	-0.11; 0.12	0.00	-0.12; 0.12
Sex (Female)			1.67	-0.07; 3.41
Education 2 (Upper secondary)			-1.76	-8.49; 4.97
Education 3 (University of applied sc.)			0.12	-6.66; 6.90
Education 4 (University)			0.52	-6.28; 7.32
R ²	0.0002		0.09	

For gender, male gender was used as a reference. For education, lowest educational level (basic education) was used as a reference.

Model 1: Unadjusted. Model 2: Adjusted for sex and educational level.

* p<.05, **p<.01, *** p<.001

b) Predicting diet quality at age 26 with depressive symptoms at age 20

	Model 1		Model 2		Model 3	
	B	95 % CI	B	95 % CI	B	95 % CI
Depression	-0.06	-0.18; 0.07	-0.09	-0.22; 0.03	-0.10	-0.21; 0.02
Gender (Female)			2.77**	0.99; 4.55	2.39**	0.63; 4.16
Education 2 (Upper secondary)			5.37	-1.54; 12.27	5.76	-1.00; 12.53
Education 3 (University of applied sc.)			6.45	-0.50; 13.41	6.43	-0.38; 13.24
Education 4 (University)			8.31*	1.33; 15.28	8.19*	1.36; 15.10
Diet at the age of 20					0.22*	0.06; 0.39
R ²	0.01		0.17		0.21	

For gender, male gender was used as a reference. For education, lowest educational level (basic education) was used as a reference.

Model 1: Unadjusted. Model 2: Adjusted for sex and educational level. Model 3: Additionally adjusted for diet at age 20.

* p<.05, **p<.01, *** p<.001

c) Interactions of group and depression when predicting diet quality at ages 20 and 26

	Diet at age 20		Diet at age 26	
	B	95 % CI	B	95 % CI
Depression	-0.01	-0.15; 0.14	-0.06	-1.03; 13.49
Sex (Female)	1.61	-0.13; 3.35	2.36	0.59; 4.14 **
Education 2 (Upper secondary)	-1.60	-8.34; 5.13	5.10	-0.81; 12.80
Education 3 (University of applied sc.)	0.14	-6.64; 6.92	6.62	-0.22; 13.46
Education 4 (University)	0.61	-6.20; 7.41	8.42	1.56; 15.29 *
Group (Intervention group)	0.96	-1.17; 3.08	1.12	-1.04; 3.27
Group*Depression	0.04	-0.20; 0.28	-0.11	-0.35; 0.13
Diet at age 20			0.22	0.06; 0.39 **
R ²	0.0002		0.22	

For gender, male gender was used as a reference. For education, lowest educational level (basic education) was used as a reference. For group, control group was used as a reference.

Analyses adjusted for sex and educational level. Analysis for diet at age 26 additionally adjusted for diet at age 20.

* p<.05, **p<.01, *** p<.001